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Comparison of right and left ventricular function and size in Duchenne muscular dystrophy

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ABSTRACT

Introduction: Right ventricular (RV) size and function in Duchenne muscular dystrophy (DMD) have not been well described. Using cardiac magnetic resonance (CMR) imaging we describe the relationship of RV and left ventricular (LV) size and function in a large DMD cohort.
Methods: Latest CMR scans of 272 patients consecutively seen at a single tertiary referral center (2011–2014) with skeletal muscle biopsy confirmed DMD were included. 1.5 and 3 Tesla CMR scanners were used. Biventricular ejection fraction (EF), end-diastolic volume index (EDVI), mass and mass index were compared across categories of LVEF.
Results: Mean age was 13.5 ± 4.9 years. 71% had normal (≥55%) LVEF while mild (EF 45–54%), moderate (EF 30–44%), and severe LV dysfunction (EF <30%) was present in 20%, 6% and 3% respectively. The correlation between RVEF and LVEF was weak. Even in patients with severe LV dysfunction, RVEF (49.7% ± 12.9%) was relatively preserved. There were no significant differences in RVEDVI and RV mass index across categories of LV function.
Conclusion: In a large DMD cohort, RVEF was relatively preserved and RV size was preserved across categories of LV dysfunction.

1. Introduction

Duchenne muscular dystrophy (DMD), an X-linked recessive disorder affecting approximately 1 in 3500 males, is the most common inherited muscular dystrophy. Symptom begins in early childhood, usually between ages 3 and 5. Muscle weakness first affects the muscles of the hips, pelvic area, thighs and shoulders, followed by involvement of the skeletal muscles in the arms, legs and trunk. By the early teens, cardiac and respiratory muscles also are affected [1]. DMD results from mutations in the dystrophin gene, a sarcolemmal protein that is abundant in both skeletal and cardiac muscle. Corticosteroids and supportive respiratory devices have improved motor and respiratory outcomes [2,3]. As a result DMD associated cardiac disease is now the leading cause of death, which typically occurs in the second to third decade of life [4,5]. DMD has generally been considered a contraindication for cardiac transplantation given the nature of the illness and underlying progressive systemic myopathy [6]. Recent advances in left ventricular assist device (LVAD) as destination therapy have now made the use of this technology feasible in DMD patients [7,8].

Abbreviations: DMD, Duchenne muscular dystrophy; BSA, Body surface area; CMR, Cardiovascular magnetic resonance; LVEDVI, Left ventricular end-diastolic volume index; RVEDVI, right ventricular end-diastolic volume index; LVEF, Left ventricular ejection fraction; RVEF, right ventricular ejection fraction; LVM, left ventricular mass; LVMI, left ventricular mass index; RVM, right ventricular mass; RVMI, right ventricular mass index; SSFP, Steady state free precession.

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Table 1
Distribution of left and right ventricular parameters by LVEF.

Parameter(mean ± SD)	Group1(n = 195)LVEF≥55%	Group 2(n = 54)LVEF45–54%	Group 3(n = 16)LVEF30–44%	Group 4(n = 7)LVEF<30%	p value*
Age (yr)	12.0 ± 3.8	16.2 ± 4.8	18.5 ± 5.0	23.0 ± 6.1	<0.001
BSA (m^2)	1.2 ± 0.3	1.6 ± 0.3	1.5 ± 0.3	1.6 ± 0.3	<0.001
LVEF (%)	64.6 ± 4.6	50.8 ± 3.1	41.9 ± 3.2	23.9 ± 4.1	<0.001
LVEDVI (mL/m^2)	68.8 ± 13.8	81.6 ± 15.3	103.6 ± 19.8	139.6 ± 22.8	<0.001
LV mass (g)	56.6 ± 16.1	81.9 ± 41.9	83.7 ± 19.6	95.2 ± 15.9	<0.001
LV mass index (g/m^2)	46.6 ± 9.4	50.6 ± 15.3	55.5 ± 12.0	58.4 ± 4.7	<0.001
RVEF (%)	63.4 ± 6.5	57.2 ± 6.2	55.2 ± 4.6	46.7 ± 12.7	<0.001
RVEDVI (mL/m^2)	68.6 ± 14.0	72.7 ± 18.1	77.6 ± 16.0	65.2 ± 24.2	0.08
RV mass (g)	16.7 ± 5.9	21.5 ± 8.4	20.4 ± 8.0	22.2 ± 7.1	<0.001
RV mass index (g/m^2)	13.4 ± 4.0	13.7 ± 5.0	13.4 ± 2.8	13.4 ± 2.8	0.95

BSA, body surface area; LV, left ventricular; RV, right ventricular; LVEF, left ventricular ejection fraction; LVEDVI, left ventricular end-diastolic volume index; RVEDVI, right ventricular end-diastolic volume index.
* Kruskal–Wallis test.

Right ventricular (RV) systolic dysfunction is believed to be a strong predictor of poor outcome in nonischemic dilated cardiomyopathies [9]. There is a paucity of data describing RV size and function in patients with DMD. At our institution and others, cardiac magnetic resonance (CMR) imaging is routinely used in the surveillance of global and regional cardiac function and to evaluate for the presence of myocardial fibrosis in patients with DMD. The purpose of the present study was to compare CMR derived biventricular ejection fraction (EF), end-diastolic volume index (EDVI), mass and mass index across categories of left ventricular (LV) systolic function in a large cohort of DMD patients. Although the same dystrophin mutation is present in RV and LV myocytes, because of the different work load experienced by the RV and LV, we hypothesized the measures of function and mass would differ.

2. Methods

2.1. Study population

Data were analyzed from latest scans of 272 DMD patients consecutively seen at a single tertiary referral center who underwent clinical CMR studies between March 2011 and October 2014. Only patients with a known diagnosis of DMD confirmed by skeletal muscle biopsy, showing absent dystrophin and/or DNA analysis demonstrating a known dystrophin mutation, were included. The Institutional Review Board approved the study.

3. Cardiac magnetic resonance imaging protocols and data analysis

CMR was conducted either on a 1.5 Tesla (T) GE Signa Excite (General Electric Healthcare; Milwaukee, WI), or Philips 3T Achieva (Philips Healthcare, Andover, MA). Scanner type was based solely on clinical availability, independent of the patient's clinical status. Cardiac functional imaging was performed using a standard retrospective ECG-gated, segmented steady state free precession (SSFP) technique and includes a short axis stack of cine SSFP images from cardiac base to apex as previously described [10,11]. (Scan parameters: 6 mm slice thickness with no gap; 1.5 mm^2 acquired in-plane resolution; field of view manipulated to maintain constant resolution for body size; 30 phases/RR interval; minimum TE; TR ~2.8 ms; Nex = 3, if free breathing) LV and RV volume, mass and EF were assessed via standard planimetry techniques using semi-automated computer software (QMASS v.6.1.5, Medis Medical Imaging Systems, Netherlands) [10,11]. Ventricular volumes, mass, and EF along with subject demographic data were tabulated for each subject, and then exported to a spreadsheet file for off-line analysis. For more detailed information, please refer to our previously published paper [12].

LVEF ≥55% was considered normal. LV dysfunction was considered to be mild (LVEF 45–54%), moderate (LVEF 30–44%) or severe (LVEF <30%).

4. Statistical methods

Data were summarized by counts and percentages for categorical variables, and means and standard deviations for continuous variables. Non-parametric Kruskal–Wallis test was used to compare more than 2 groups [13]. Spearman's rank correlation was used to assess the correlations between RVEF and LVEF, RVEDVI and LVEDVI, RV and LV mass and mass index [14]. The statistical significance was set at the nominal $\alpha = 0.05$ level. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0. (Armonk, NY: IBM Corp.)

5. Results

Over the study period majority (~70%) scans were performed using the 1.5T GE Signa Excite (General Electric Healthcare; Milwaukee, WI) while the remainder were performed using the Philips 3T Achieva (Philips Healthcare, Andover, MA).

6. Patient stratification

Of the 272 boys (mean age 13.5 ± 4.9 years), 195/272 (71.7%) had normal LVEF while 54/272 (19.9%) had mild, 16/272 (5.9%) moderate and 7/272 (2.6%) had severe LV dysfunction. Table 1 describes the distribution of biventricular EF, EDVI, mass and mass index by categories of LVEF. There was no difference in RVEDVI and right ventricular mass index (RVMI) across categories of LV function.

7. Correlation of LVEF and RVEF

A wide range of LVEF was observed (17.7% to 78.0%) while RVEF ranged from 33.1 to 83.8%. The correlation between LVEF and RVEF for all patients was moderate to strong ($r = 0.62$; $p < 0.001$) (Fig. 1). When stratified by LVEF, the correlation was not significant in patients with mild and severe LV dysfunction (Table 2).

8. Comparison of LV and RV size

A wide range of LVEDVI was observed (34.8 to 175.2 mL/m^2). RVEDVI ranged from 31.6 to 135.7 mL/m^2. The correlation between LVEDVI and RVEDVI was strong for all scans ($r = 0.73$; $p < 0.001$) (Fig. 2) as well as in patient with mild to moderate LV dysfunction (Table 2). There was no significant correlation in patients with severe LV dysfunction.

RV and LV mass demonstrated strong correlation for all scans ($r = 0.70$; $p < 0.001$) while RVMI and LVMI showed moderate cor-